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PEDIATRIC-ONSET NEUROMYELITIS OPTICA SPECTRUM DISORDER: CLINICAL AND RADIOLOGICAL PROFILES WITH SHORT-TERM OUTCOMES IN A TERTIARY CARE CENTER IN PAKISTAN (RETROSPECTIVE CHART REVIEW)

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Pediatric NMOSD, Neuromyelitis Optica Spectrum Disorder, Aquaporin-4 (AQP4) antibody, Myelin Oligodendrocyte Glycoprotein (MOG) antibody

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Abstract

Background: *Pediatric Neuromyelitis Optica Spectrum Disorder (NMOSD) is rare and poorly characterized in Pakistan, with only isolated case reports published to date.*

Objective: *To describe the clinical, radiological, and serological profiles with short-term outcomes of pediatric NMOSD at a tertiary care center in Pakistan.*

Methods: *This retrospective study reviewed 122 pediatric patients with acute demyelinating disorders at Aga Khan University Hospital, Karachi (2020–2024). Nine patients meeting the 2015 IPND criteria for NMOSD were included. Demographics, clinical features, MRI findings, CSF analysis, serological profiles, treatment strategies, and EDSS scores at discharge and three months were analyzed.*

Results: *The mean age at presentation was 10.6 years, with a slight male predominance (1.25:1). AQP4 antibodies were identified in 22%, MOG antibodies in 22%, and 56% remained seronegative. All patients phenotypically had both optic neuritis and transverse myelitis, with LETM present in 100% on spinal MRI. Brainstem involvement was observed in 44% of patients. AQP4-positive patients demonstrated the most severe outcomes (mean discharge EDSS: 7.5), while MOG-positive patients achieved full recovery (EDSS: 0) at three months. No deaths occurred during the study period.*

Conclusion: *This first comprehensive Pakistani pediatric NMOSD cohort highlights a low AQP4-positivity rate, high brainstem involvement, and variable outcomes across serological subgroups, reinforcing the need for thorough clinical, radiological, and immunological evaluation.*

INTRODUCTION

Background:

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disorder affecting central nervous system structures, notably optic nerves, spinal cord, and brainstem, commonly leading to conditions such as optic neuritis (ON), transverse myelitis (TM), or area postrema syndrome (APS). [(1)] While pediatric NMOSD accounts for only 3-5% of all cases, it poses significant diagnostic and treatment challenges due to its diverse clinical presentation. The disorder is commonly associated with anti-aquaporin-4 (AQP4) antibodies; however, some

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patients may test negative for AQP4 and instead test positive for myelin oligodendrocyte glycoprotein (MOG) antibodies. [2, 3] AQP4-IgG testing in serum shows a sensitivity of 58–76% and specificity ranging from 85-99%, supporting its diagnostic utility. [4]

In pediatric patients, NMOSD tends to be less severe than in adults, with a higher likelihood of monophasic disease course and relatively less motor impairment. However, visual impairment remains a major concern. [5] Six core clinical characteristics define NMOSD, which include

1. Optic neuritis (ON)
2. Longitudinally extensive transverse myelitis (LETM)
3. Area postrema syndrome (APS)
4. Acute brainstem syndrome (ABS), excluding APS
5. Symptomatic narcolepsy or acute diencephalic syndrome with NMOSD-typical diencephalic lesions on MRI
6. Acute cerebral syndrome with NMOSD-typical brain lesions on MRI

According to the International Panel for NMO Diagnosis (IPND) 2015 revised guidelines, a diagnosis of NMOSD requires one core clinical feature in the presence of AQP4 antibodies. If antibodies are absent, at least two core features must be present, one of which must be ON. TM, or APS. [6] The term "longitudinally extensive" was applied to both ON and TM. Optic neuritis involving more than half the length of optic nerve or optic chiasm was labeled as longitudinally extensive optic neuritis (LEON), while lesions involving three or more contiguous spinal segments were defined as longitudinally extensive transverse myelitis (LETM). [1] Patients presenting with isolated LETM should undergo evaluation for ON, including visual acuity assessment and visual evoked potentials (VEPs), as sub clinical ON has been observed. Conversely, patients presenting with ON should also be assessed for spinal cord involvement, given the potential for asymptomatic LETM. [1]

Early and accurate diagnosis is essential to prevent disability. High-dose intravenous corticosteroids are typically the initial treatment approach, with intravenous immunoglobulin (IVIG) or plasmapheresis considered for patients unresponsive to steroids. Maintenance therapy often includes low-dose steroids and azathioprine (AZP), a steroid-sparing agent. In more severe cases, rituximab, a monoclonal antibody, may be used. Additional long-term management options include cyclophosphamide (CYC) and mycophenolate mofetil (MMF). [7, 8] This observational study aims to contribute to the growing body of knowledge on pediatric NMOSD, focusing on clinical presentation, treatment strategies, and outcomes. By providing detailed patient analysis, this study emphasizes the importance of tailored therapeutic approaches and the potential for improved patient outcomes through early intervention.

Study Method

This retrospective observational study was conducted at Aga Khan University Hospital, Karachi, Pakistan. Records were reviewed of 114 pediatric patients who presented with acute demyelinating syndromes, including ON, TM, acute disseminated encephalomyelitis (ADEM), multiple sclerosis (MS), and NMOSD, between January 2020 and December 2024.

The study was approved by the Institutional Ethics Committee (ERC # 2024-10513-31297). Given the retrospective nature of the study and anonymized data usage, written consent was not required. However, consent was obtained via telephone from caregivers to use anonymized patient information. The patients' medical records and outpatient follow-up data were reviewed retrospectively.

Children under 18 years of age who met the 2015 IPND criteria for NMOSD were included in the study. We recorded their demographic information and presenting features, including visual symptoms such as blurry vision and diplopia, and neurological deficits such as paraplegia, hemiplegia, headache, vomiting, vertigo, encephalopathy, and seizures.

Investigations involved brain MRI scans with orbital protocols and the entire spine using contrast. Cerebrospinal fluid (CSF) analysis was conducted for all patients unless there were contraindications. We reviewed detailed CSF reports, assessed serum AQP4 antibodies, and

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analyzed paired CSF and serum oligo clonal bands (OCBs), while also checking for serum MOG antibodies to identify potential MOG-associated disorders. Additionally, most patients underwent testing for systemic autoimmune antibodies, including antinuclear antibodies (ANA) and anti-DNA antibodies. All patients received a fundoscopic examination and VEP as part of their diagnostic evaluation.

The disease was divided into two categories: seropositive and seronegative. Seropositive patients had either anti-AQP4 antibodies or MOG antibodies in their serum, while seronegative patients lacked both types of antibodies. Acute treatments included pulsed therapy with methylprednisolone, IVIG, or plasmapheresis. Maintenance therapy options included oral steroids, AZP, and MMF.

Outcomes were evaluated using the Extended Disability Status Scale (EDSS) score at the time of discharge and again three months after presentation, or following a relapse if it occurred within the first three months. The EDSS score measures disability in MS and or NMOSD, it ranges from 0 (normal neurological exam) to 10 (death due to MS).

- **0–4.5**: Patient is fully ambulatory; scores reflect increasing levels of neurological impairment without walking aid.
- **5.0–6.5**: Walking becomes impaired; assistance such as canes or crutches may be needed.
- **7.0–9.5**: Patient is largely wheelchair-bound or bedridden with varying degrees of independence.
- **10**: Death.

Though widely used, it is limited by its focus on mobility and under representation of other functional impairments.

Results

During a five-year study period, a total of 114 pediatric cases of acute demyelinating disorders, such as ON, TM, MS, and NMOSD, were identified at Aga Khan University Hospital. Among these cases, nine patients met the 2015 IPND criteria for NMOSD and were included in this study.

Of the nine patients, two (22%) tested positive for AQP4 antibodies, two (22%) were positive for MOG antibodies, and five (56%) were seronegative. The gender distribution was balanced, with five males and four females, resulting in a male-to-female ratio of 1.25:1. Among the nine patients, mean age at presentation was 10.6 years (SD 3.8).

All patients had evidence of ON; five (cases 3, 4, 5, 6, and 9) presented with visual symptoms, while four (cases 1, 2, 7, and 8) had asymptomatic ON diagnosed via abnormal VEP findings. Seven patients presented with limb weakness (paraplegia), and all had radiological evidence of LETM. Both AQP4-positive patients (cases 1 & 2) presented with paraplegia. Among MOG-positive patients, case 3 presented with bilateral vision loss, and case 4 presented with paraplegia and brainstem symptoms, including eye pain on movement, diplopia, and vertigo, along with headache and vomiting. The seronegative group showed diverse clinical presentations: two (cases 7 & 8) had paraplegia, while two (cases 6 & 9) presented with both visual symptoms and paraplegia along with fever, vomiting, and headache, and one (case 5) had isolated vision loss. Phenotypically, all nine patients had both ON and TM. Acute brainstem syndrome was noted in both MOG-positive patients (cases 3 & 4) and in two (cases 8 & 9) seronegative patients.

Radiological assessments revealed abnormal brain MRI findings in six patients, while three patients, one AQP4-positive (case 1) and two seronegative (cases 6 & 7), had normal brain MRIs. All patients exhibited abnormal MRI results for their spines. Additionally, radiological evidence of ON was observed in one MOG-positive patient (case 3) and in two seronegative patients (5 & 9). The MOG-positive patient (case 3) exhibited bilaterally thickened optic nerves, while two seronegative patients (cases 5 and 9) showed bilateral optic nerve thinning. One of them (case 9) also demonstrated optic chiasm involvement. No radiological evidence of optic nerve involvement was found in the six remaining patients. Four patients, including two MOG-positive (cases 3 & 4) and two seronegative individuals (cases 8 & 9), exhibited radiological signs of acute brainstem

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involvement. These signs included lesions in the periaqueductal region, tectal plate, pons, and cerebral peduncles. Thalamic involvement, which is a feature associated with the diencephalon, was observed in one MOG-positive patient (case 3); however, it was not accompanied by any related symptoms.

Post-contrast enhancement was noted in both AQP4-positive patients in the spinal cord, in one MOG-positive patient (case 3) in the optic nerve (extending to the chiasm), and in four of five seronegative patients. Among the seronegative cases, one patient (case 5) showed questionable optic nerve enhancement, while three exhibited patchy enhancements in the spinal cord.

VEPs were abnormal in all but one seronegative patient (case 9), in whom ON was diagnosed on clinical symptoms and MRI findings. Fundoscopic examination was normal in both AQP4-positive patients, one MOG-positive patient (case 4), and two seronegative patients (cases 7 & 8). However, bilateral optic disc pallor was noted in one MOG-positive (case 3) and two seronegative patients (5 & 9).

CSF analysis revealed pleocytosis in three patients, one from each group (cases 2, 4, and 8). OCBs were present in both CSF and serum in all but one seronegative patient (case 6). Autoimmune screening was negative in most cases.

All patients received high-dose IV methylprednisolone followed by oral prednisolone and AZP for long-term immunosuppression. Both AQP4-positive patients were treated aggressively with plasmapheresis, and one (case 1) also received IVIG; neither had a relapse within the three-month follow-up period. MOG-positive patients responded well to steroids; however, one patient (case 3) who initially presented with optic neuritis relapsed after two months with similar symptoms and required IVIG. Among seronegative patients, three (cases 6, 8, & 9) required plasmapheresis during acute management. Two of these three (cases 6 & 9) had both visual symptoms and paraplegia, and one (case 8) had paraplegia alone. At discharge, EDSS scores were highest among AQP4-positive patients (mean score: 7.5), followed by seronegative patients (mean score: 6.8, range: 2.0–8.5), and lowest among MOG-positive patients (mean score: 3.5). Patients presenting with paraplegia (case 4) had more severe disability compared to those with optic neuritis alone. At the three-month follow-up, most patients showed significant improvement, except for two AQP4-positive and two seronegative patients (cases 7 & 9) who continued to have significant functional limitations. Both MOG-positive patients had an EDSS score of zero at three months, including one (case 3) assessed after relapse. No deaths or cases requiring ventilatory support were observed during the study period.

Discussion

Pediatric Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune neuroinflammatory condition, with limited literature available globally, particularly from Southeast Asia, where only a few studies have been published, [2, 6], and in Pakistan, only isolated case reports have been published to date. [9-11] This study represents the first comprehensive report from Pakistan detailing the clinical features, serological profiles, radiological findings, treatment strategies, and short-term outcomes of pediatric NMOSD.

The mean age of onset in our cohort (10.6 years) aligns closely with data from international pediatric cohorts, such as the U.S. Pediatric Multiple Sclerosis Network, where a mean age of 10.2 years has been reported. [12] In contrast to the well-established female predominance in NMOSD (female-to-male ratio up to 4:1), [13] our cohort showed a slight male predominance (1.25:1). This gender pattern is similar to that reported in other South Asian pediatric NMOSD series, [6] suggesting potential ethnic or geographic variability.

Serological profiling revealed that AQP4 antibody positivity in 22% (2/9) of patients, considerably lower than the 65% reported in Western pediatric NMOSD cohorts. [13] Notably, both AQP4-positive patients were at the extremes of age (youngest and oldest), although the small sample size limits the broader conclusion. In our cohort, MOG antibodies were identified in another 22% (2/9), while the majority (56%, 5/9) remained seronegative. This distribution mirrors findings

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from Indian cohorts, where MOG positivity and seronegative status are more common than AQP4 positivity. [6] These results emphasize the heterogeneity of NMOSD in children, highlighting the diagnostic challenges and the necessity for thorough clinical, radiological, and immunological assessment in pediatric patients.

Among the AQP4-positive patients in our cohort, paraplegia was the predominant presenting symptom. This contrasts with findings from a large multinational pediatric NMOSD cohort, where visual symptoms were the most common initial manifestation (29%; 20 of 67 patients). [13] Both these patients have asymptomatic ON, diagnosed by abnormal VEP findings, so phenotypically, they both have LETM and ON.

In the MOG-positive group, one patient (case 3) presented with bilateral blurring of vision, while the other (case 4) had paraplegia, and both showed clinical or radiological signs of brainstem involvement. This is consistent with observations from the Indian cohort, where two of four MOG-positive patients presented with visual symptoms and two with paraplegia. [6] However, in contrast to our findings, brainstem involvement was not reported in that cohort, and only one patient had features of cerebral syndrome. The presence of brainstem lesions in both of our MOG-positive patients underscores the need for detailed neuroimaging in suspected MOGAD cases, especially when symptoms are multifocal or non-localizing.

The seronegative group demonstrated the greatest clinical heterogeneity. Two patients (2/5; 40%) (cases 7 & 8) had isolated paraplegia, another two (2/5; 40%) presented with paraplegia accompanied by blurred vision (unilateral in case 6 and bilateral in case 9), and one (1/5; 20%) (case 5) had isolated blurry vision. This pattern partially mirrors the Indian cohort's seronegative subgroup, where combined paraplegia and blurry vision were most frequent (42.8%), followed by isolated paraplegia (28.5%) and a single case of isolated blurry vision. [6] The overlap in presentations reinforces the importance of thorough investigation in seronegative cases, as diagnosis and treatment cannot rely on serology.

Brainstem involvement was evident in 4 out of 9 patients (44%), a markedly higher proportion than the 4.5% reported in earlier pediatric NMOSD cohorts. [13] Additionally, diencephalic (thalamic) involvement was observed in one patient, consistent with previous reports. [13]

In our cohort, MRI brain abnormalities were observed in 66% of patients, closely aligning with previous reports (60%). [14] In contrast, MRI spine abnormalities were seen in all patients (100%), with LETM being the predominant finding. This is significantly higher than reported in earlier literature, underscoring the diagnostic importance of spinal imaging in pediatric NMOSD. Gadolinium (Gd) enhancement was noted in 50% of patients with abnormal brain MRIs (3/6) and 55% with spinal involvement (5/9). Notably, 100% of AQP4-positive patients in our cohort demonstrated Gd enhancement of spinal lesions, supporting its role as a marker of active inflammation. These findings emphasize the utility of contrast-enhanced MRI in assessing disease activity, particularly in antibody-positive patients.

According to the 2015 IPND criteria and subsequent literature, LEON and optic chiasm involvement are hallmark features in AQP4-positive NMOSD. [1] However, in our study, neither of the two AQP4-positive patients exhibited optic nerve involvement on MRI. In contrast, MOG-positive (case 3) and 2 seronegative patients (cases 5 & 9) displayed optic pathway abnormalities, including signal changes extending to the optic chiasm, with Gd enhancement except for one seronegative patient (case 9), who has non-enhancing lesions. Brain MRI findings in AQP4-positive patients were either normal or limited to non-specific cerebral white matter lesions, diverging from typical patterns described in literature. Furthermore, while diffuse spinal cord involvement is often associated with AQP4-positive NMOSD, [1] neither of our AQP4-positive cases showed complete cord involvement, although both demonstrated LETM with Gd enhancement. In contrast, one MOG-positive patient (case 3) and one seronegative patient (case 6) exhibited inflammation of the entire spinal cord, a finding more commonly associated with

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AQP4-positive NMOSD but occasionally seen in MOGAD. [1]

Both MOG-positive patients (cases 3 & 4) had abnormal brain MRIs featuring non-specific white matter lesions and brainstem involvement, a higher frequency than reported in an Indian cohort. [6] Notably, only one of these MOG-positive cases (case 3) demonstrated thickened optic nerves, consistent with previously described imaging features in MOGAD. [1]

Among seronegative patients, neuroimaging revealed classic NMOSD features. LETM was universally present 5/5, typically involving the cervical and thoracic spinal cord. Brain MRIs often showed optic pathway abnormalities and brainstem lesions. 2 out of 5 (40%) (cases 5 & 9) demonstrated significant optic nerve involvement on MRI. Both showed bilateral thinning of the optic nerves, suggestive of chronic demyelinating damage. One patient (case 5) exhibited involvement of the posterior intraorbital and canalicular segments, while the other (case 9) showed extension of abnormal signals to the optic chiasm. However, gadolinium enhancement was observed in only one (case 5) of these cases, and even then, the enhancement was questionable, indicating limited evidence of active inflammation. Brainstem involvement, such as signal changes in the periaqueductal region, tectal plate, medial temporal lobes, and hemi-pons, was found in 2/5 (cases 8 & 9). This suggests that seronegative NMOSD can present with radiological features indistinguishable from seropositive forms. Importantly, the frequency of brainstem involvement in our seronegative cohort was markedly higher than in prior pediatric series, where such findings were considered rare. [13] This observation highlights that neuroimaging is crucial for diagnosing pediatric NMOSD, especially when serological results are unclear, which leads to the prompt initiation of immunosuppressive therapy.

CSF pleocytosis with lymphocytic predominance is a recognized feature of NMOSD, [14] yet in our cohort, it was observed in only 33% (3/9) of patients—one each from the AQP4 (case 2), MOG (case 4), and seronegative (case 8) groups. Although OCBs are not diagnostic for NMOSD, their presence exclusively in CSF may help differentiate NMOSD from MS. Interestingly, OCBs were found in 88% of our patients, which is notably higher than previously reported figures. [3] However, the presence of OCBs in both CSF and serum suggests a systemic inflammatory process rather than isolated CNS involvement.

Fundoscopy is a valuable diagnostic tool in differentiating NMOSD, MOGAD, and MS. In our cohort, fundoscopy was normal in six patients, including both AQP4-positive cases, while optic disc pallor was observed in three patients (one MOG-positive (case 3) and two seronegative (cases 5 & 9)).

VEPs provide diagnostic insight for ON, showing reduced amplitudes and prolonged latencies; in severe cases, responses may be absent. Prolonged latencies may also reflect subclinical optic nerve involvement. [15] VEPs were abnormal in all but one patient (case 9) in our cohort; this exception had radiological evidence of optic nerve involvement.

All patients received intravenous methylprednisolone for five days as first-line treatment. Both AQP4-positive patients (cases 1 & 2) were unresponsive to steroids and required plasmapheresis. One of them (case 1) also failed to respond to IVIG and was ultimately managed with plasmapheresis. These patients had the poorest outcomes, with a mean EDSS score of 7.5 at discharge, improving only slightly to 5.25 at three months. This highlights the severe and refractory nature of AQP4-positive NMOSD, consistent with previous reports. [14] Notably, none experienced relapses within the first three months, which contrasts with the typically relapsing nature of AQP4-NMOSD. However, this may be due to the short duration of follow-up.

MOG antibody-positive patients (cases 3 & 4) showed good initial responses to steroid therapy. One patient (case 3) experienced a relapse with visual symptoms two months after the initial episode. This patient responded well to IVIG, aligning with existing literature. [8] At discharge, MOG-positive patients had a mean EDSS score of 3.5. The patient with ON (case 3) had the best EDSS score of 1 among all participants, although he later relapsed, challenging prior findings suggesting a correlation between better EDSS

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scores and fewer relapses. [16] Following relapse, his EDSS score improved to zero after three months of follow-up. Previous studies have reported EDSS ≥3 in 43.2% of MOGAD patients, especially those presenting with ON. [13]

Seronegative patients were managed similarly to seropositive cases, emphasizing the need for aggressive treatment. In our cohort, 2 of 5 (cases 5 & 7) responded to methylprednisolone alone, while the remaining (cases 6, 8, & 9) required plasmapheresis. Those (cases 6, 7, 8 & 9) presenting with paraplegia had the worst outcomes, [16] with a mean EDSS of 8 at discharge and 3.6 at three months. In contrast, a patient (case 5) with ON had a discharge EDSS of 2, which improved to 0 by three months. Although the EDSS is the standard tool for evaluating neurological disability in NMOSD, it may not fully capture visual or cognitive deficits, which are clinically significant in pediatric cases. [17]

Azathioprine was used for maintenance therapy in all patients. Previous studies have demonstrated up to an 89% reduction in relapse rate with azathioprine over 18 months, supporting its use in long-term management. [3, 13]

Conclusion

Our findings emphasize the diverse clinical spectrum of pediatric NMOSD. Patients who are positive for AQP4 experienced more severe disease and poorer short-term outcomes, even with aggressive treatment. In contrast, patients with MOG antibodies generally had better responses, although they can still experience relapses. Additionally, seronegative patients exhibited a wide range of clinical presentations. These insights provide valuable regional data to enhance the global understanding of pediatric NMOSD and support the development of standardized treatment protocols.

Limitations

This study has certain limitations. The small sample size reflects the rarity of pediatric NMOSD, and the single-center design limits the generalizability of the findings to a broader population. MOG antibody testing was not performed in all patients, as its clinical relevance has only recently been established in diagnostic protocols. Furthermore, due to the retrospective nature of the study, with follow-up limited to three months, long-term outcomes, relapse patterns, and sustained treatment responses could not be adequately assessed

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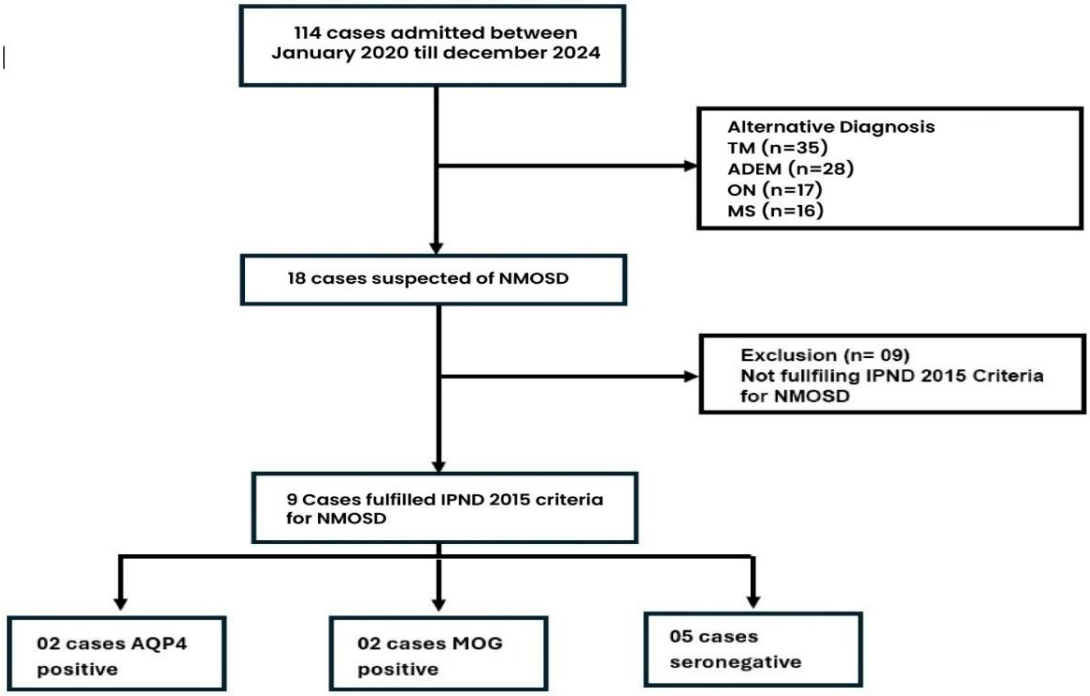

Figure 1: Flow diagram summarizing diagnostic process and classification of NMOSD cases (January 2020 – December 2024) according to IPND 2015 criteria.

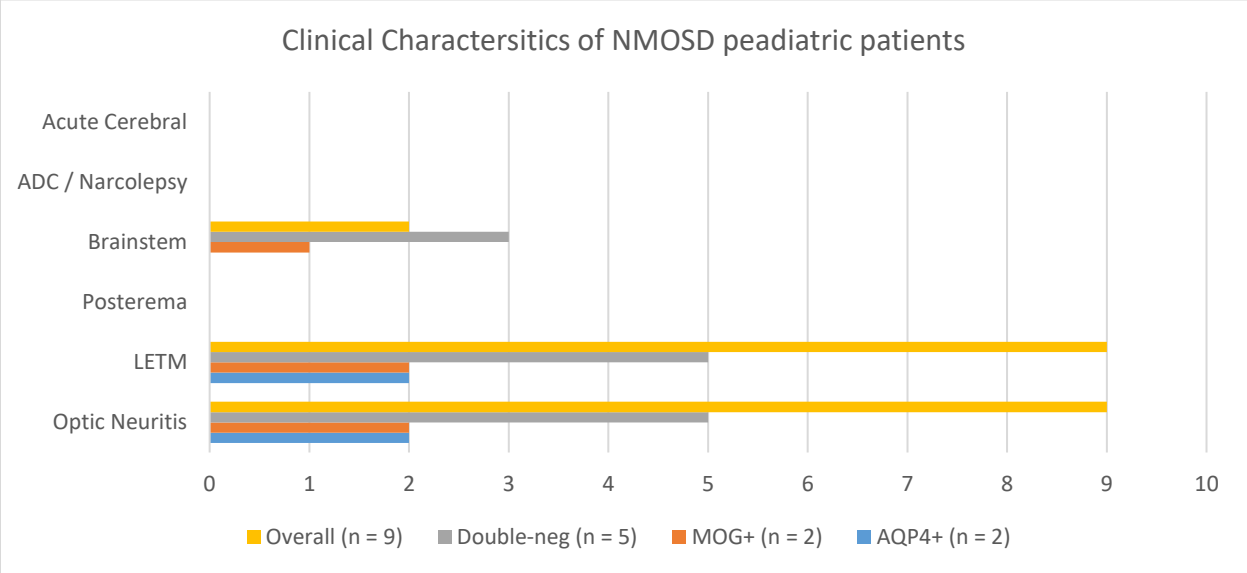

FIGURE 2: Clinical characteristics of paediatric NMOSD patients (n = 9). Distribution of clinical presentations among overall patients and according to serological status (double-negative, MOG antibody-

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positive, and AQP4 antibody-positive). LETM = longitudinally extensive transverse myelitis; ADC = acute disseminated encephalomyelitis

Variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Age & Gender	4y5m, M	17y, F	7y, M	13y, F	12y, F	10y, M	14y, M	9y, M	9y, F
Presenting Symptom	Paraplegia	Paraplegia	Bilateral vision loss	Paraplegia, vertigo, headache, vomiting, diplopia and pain of eye movements	Bilateral vision loss	Vision blurring (Left eye), paraplegia, fever, vomiting, headache	Paraplegia	Paraplegia	Blurry vision, paraplegia, fever& vomiting
Phenotype	TM and ON (silent)	TM and ON (silent)	ON, silent TM, ABS	TM, ABS, & ON (Silent)	ON & TM (Silent)	ON & TM	TM & silent ON	TM, silent ON, ABS	TM, ON, ABS,
Serology	AQP4 Positive	AQP4 Positive	MOG Positive	MOG Positive	Seronegative	Seronegative	Seronegative	Seronegative	Seronegative
MRI Brain (Abnormal signals)	Normal	Occipital WM, parietal lesion	Thick Optic nerves, WM, brainstem, thalami and basal ganglia	WM, brainstem lesions	Left Optic nerve Thinning of both Optic nerves	Normal	NA	Subcortical WM, hemi-pons	Optic pathways, medial temporal, brainstem
MRI Spine	LETM (C1-T10)	LETM (C2–T12)	LETM (C2-T2)	LETM (C3-L1)	LETM (C1-C6)	LETM (C2-T10)	LETM (C2–T3)	LETM (C2-L1)	LETM (C1-T1)
Gd Enhancement	Yes	Yes, patchy of cord	Yes, optic nerves to chiasma	No	Questionable optic nerve	Yes	No	Yes	Patchy

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Eye Exam	Normal	Normal	Disc pallor	Normal	Disc pallor	RAPD positive	Normal	Normal	Disc pallor (R>L)
VEP	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Normal
OCB	Present in both	Present in both	Present in both	Present in both	Present in both	Absent	Present in both	Present in both	Present in both
CSF Pleocytosis	NA	WBC 32, Lym 95%	WBC 6	WBC 86, Lym 95%	WBC 01	WBC 4	WBC 4	WBC 30, Lym 90%	WBC 1
Autoimmune Workup	NA	ANA, DNA, ENA Negative	ANA, ENA Negative	ANA, DNA, ENA Negative	ANA, DNA Negative	ANA, DNA Negative	NA	ANA Negative	ANA, DNA Negative
Acute Treatment	IVMP + IVIG, PLEX	IVMP + PLEX	IVMP, IVIG on relapse	IVMP	IVMP	IVMP + PLEX	IVMP	IVMP + PLEX	IVMP + PLEX
EDSS Discharge	6.5	8.5	1.0	6.0	2.0	6.5	8.5	8.5	8.5
Relapse			After 2 months with ON						
Long-term Treatment	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine	Steroids + Azathioprine
EDSS 3mo	5.5	5	0.0	0.0	0.0	2.0	6.0	1.0	5.5

Table1 : Showing Demographic, clinic-radiological characteristics, treatment and outcome. AQP4, Aquaporin 4; MOG, Myelin oligodendrocyte glycoprotein; TM, Transverse myelitis; ON, Optic neuritis; ABS, Acute brainstem syndrome; WM, white matter; NA, not available; Gd, gadolinium; RAPD, Relative afferent pupillary defect; R, Right; L, left; VEP, Visual evoked potential; OCB, Oligo clonal bands; CSF, Cerebrospinal fluid; WBC, white blood cell; Lym, lymphocyte; ANA, Antinuclear antibody, DNA, Deoxyribonucleic acid; ENA, extractable nuclear antigen; IVMP, Intravenous methylprednisolone; PLEX, Plasmapheresis; IVIG, intravenous immunoglobulin; EDSS, Extended Disability status scale.

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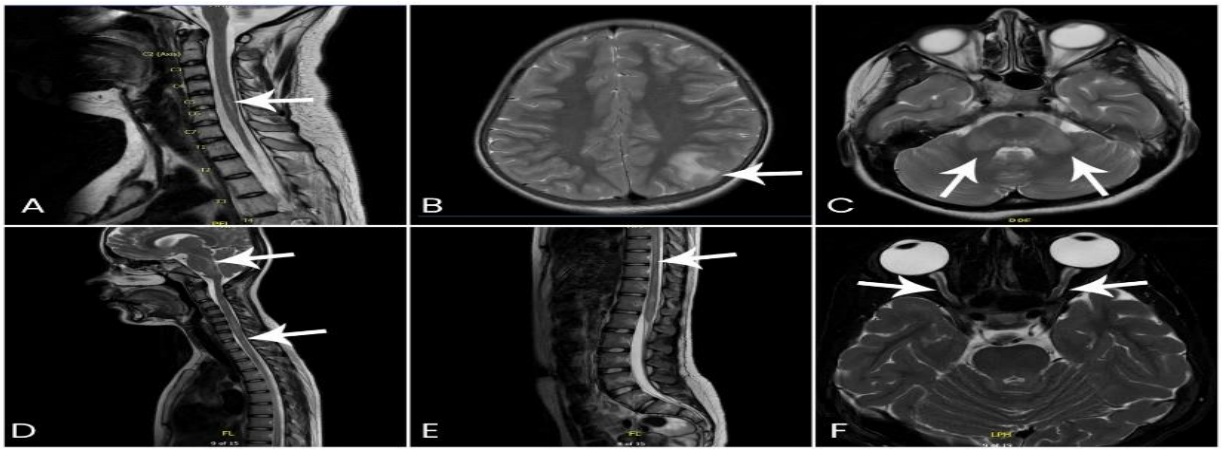

Figure 3: MRI findings of Neuromyelitis optica spectrum disorder (NMOSD) patients; (A), Case 2, MRI spine, hyper intense signals in spine. (B-E) Case 4, MRI brain showing hyperintense signals at left parieto-occipital and bilateral middle cerebral peduncles and MRI spine sagittal view showing hyper intense signals at posterior pons, and in spine from C3 to L1 ; (F) case 9, MRI Brain showing bilateral thinning of optic nerves.

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